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     (FILE 'HOME' ENTERED AT 11:56:21 ON 26 MAR 2003)

     FILE 'EUROPATFULL, PCTFULL, USPAT2, WPIDS' ENTERED AT 11:56:59 ON 26 MAR
     2003

     FILE 'EUROPATFULL, PCTFULL, USPATFULL, USPAT2, WPIDS' ENTERED AT
11:57:09
     ON 26 MAR 2003
L1         22391 S RETINOL OR RETINAL OR RETINYL
L2             0 S L1(S)CIMBAZOLE

     FILE 'CAPLUS' ENTERED AT 12:36:56 ON 26 MAR 2003

     FILE 'REGISTRY' ENTERED AT 12:37:04 ON 26 MAR 2003
                E CIMBAZOLE/CN
                E CLIMBAZOLE

     FILE 'EUROPATFULL, PCTFULL, USPATFULL, USPAT2, WPIDS' ENTERED AT
12:39:39
     ON 26 MAR 2003
L3            35 S L1(S)CLIMBAZOLE

     FILE 'USPATFULL' ENTERED AT 12:40:30 ON 26 MAR 2003
L4            11 S L3
L5             1 S L4 NOT PY>=2000
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L5 ANSWER 1 OF 1 USPATFULL
ACCESSION NUMBER: 1998:14487 USPATFULL
TITLE: Skin care compositions containing fatty acid amides, azoles, and retinol or retinyl ester
INVENTOR(S): Granger, Stewart Paton, Paramus, NJ, United States
Rawlings, Anthony Vincent, Warrington, England
Scott, Ian Richard, Allendale, NJ, United States
PATENT ASSIGNEE(S): Elizabeth Arden Co., Division of Conopco, Inc., New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5716627		19980210	
APPLICATION INFO.:	US 1996-638074		19960425	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Venkat, Jyothsan
LEGAL REPRESENTATIVE: Mitelman, Rimma
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 958
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD LINOLEOYL-DEA, **CLIMBAZOLE** AND **RETINOL** SYNERGISTICALLY ENHANCED KERATINOCYTE PROLIFERATION AND INHIBITED DIFFERENTIATION
DETD A. The effect of linoleoyl-DEA, **climbazole** and **retinol** on incorporation of .sup.3 H-thymidine was examined. The results that were obtained are summarized in Table 3A.
DETD TABLE 3A

EFFECT OF **RETINOL**, **CLIMBAZOLE** AND LINOLEOYL-DEA ON KERATINOCYTE THYMIDINE INCORPORATION

mean Thymidine incorp/.mu.g protein	p value vs	p value vs	p value vs	
4845 .+-. 95 (130%)	0.001	0.001	--	* = 0.006 @ = 0.004
2.5 .times. 10.sup.8 M **Retinol**				
3788 .+-. 57 (102%)	0.275	--	0.001	* = 0.043 @ = 0.090
2.5 .times. 10.sup.8 M ROH + 10.sup.8 M.	.	.	--	@ = 0.626
2.5 .times. 10.sup.8 M ROH + 10.sup.9 M				
4056 .+-. 160 (109%)	0.048	0.090	0.004	* = 0.626
Climbazole			--	
2.5 .times. 10.sup.8 M ROH + 10.sup.8 M LADEA				

4781 .+-. 196 (129%)
0.002
0.002
0.697
* = 0.023
+ 10.sup.9 M **Climbazole** @ = 0.015

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n = 3
* = p value vs 2.5 .times. 10.sup.8 M ROH + 10.sup.8 M LADEA
@ = p value vs 2.5 .times. 10.sup.8 M ROH + 10.sup.9 M **Climbazole**

DETD . . . retinoic acid significantly increased keratinocyte thymidine incorporation by 30% over the ethanol control and by 28% over the 2.5.times.10.sup.-8 M **retinol** treatment. Both 2.5.times.10.sup.-8 M **retinol**+10.sup.-8 M linoleamide-DEA and 2.5.times.10.sup.-8 M **retinol**+10.sup.-9 M **climbazole** had a significant stimulatory effect on keratinocyte proliferation over the control and **retinol** on its own. However the combination of 2.5.times.10.sup.-8 M **retinol**+10.sup.-8 M linoleamide-DEA+10.sup.-9 M **climbazole** significantly increased keratinocyte proliferation over both the ethanol and the 2.5.times.10.sup.-8 M **retinol** treatments by 29% and 27% respectively. Most significantly the combination of 2.5.times.10.sup.-8 M **retinol**+10.sup.-8 M linoleamide-DEA+10.sup.-9 M **climbazole** also significantly increased keratinocyte proliferation over both the 2.5.times.10.sup.-8 M **retinol** +10.sup.-8 M linoleamide-DEA and 2.5.times.10.sup.-8 M **retinol** +10.sup.-9 M **climbazole** treatments by 17% and 20% respectively. **Retinol**, linoleamide-DEA and **climbazole** therefore, act synergistically to increase keratinocyte proliferation to levels which closely resemble the stimulatory effect of retinoic acid.

DETD TABLE 3B

EFFECT OF **RETINOL**, **CLIMBAZOLE** AND LINOLEOYL-DEA ON KERATINOCYTETGASE LEVELS

	mean TGase/DNA .times. 10.sup.4 .+-. s.d (%)	p value vs. . . (29%)	p value	p value
2.5 .times. 10.sup.9 M RA	0.84 .+-. 0.59 (55%)	0.027	0.000	0.000
2.5 .times. 10.sup.9 M **Retinol**	1.96 .+-. 0.33 (129%)	0.553	0.000	0.000
2.5 .times. 10.sup.9 M ROH + 10.sup.8 M LA-DEA	1.59 .+-. 0.28 (105%)	0.000	--	0.000
2.5 .times. 10.sup.9 M ROH + 10.sup.8 M **Climbazole**	1.66 .+-. 0.42 (109%)	0.000	0.360	--
2.5 .times. 10.sup.9 M ROH + 10.sup.8 LA-DEA + 10.sup.8 M **Climbazole**	1.27 .+-. 0.51 (83%)	0.000	0.000	0.000
2.5 .times. 10.sup.9 M ROH +10.sup.8 M LA-DEA				

1.10 = 0.40 (72%)
0.009 0.000 0.000 0.000

+ 10.sup.7 M **Climbazole**

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n = 6

DETD . . . the more dilute 2.5.times.10.sup.-9 M retinoic acid was not as effective but still inhibited TG1 levels by 55%. 2.5.times.10.sup.-9 M **retinol**, 2.5.times.10.sup.-9 M **retinol**+10.sup.-8 M LADEA and 2.5.times.10.sup.-9 M **retinol**+10.sup.-8 M **climbazole** had no inhibitory effect on the keratinocyte TG1 level. However 2.5.times.10.sup.-9 M **retinol**+10.sup.-8 M LADEA+10.sup.-8 M **climbazole** significantly repressed keratinocyte TG1 to 83% of control levels. This inhibition was significantly greater than the control, ROH alone, ROH+LADEA and ROH+ **climbazole** indicating that the three ingredients, i.e., ROH, LADEA and **climbazole** act synergistically to inhibit keratinocyte TG1 levels. This effect was even greater when the **climbazole** concentration was increased by 10.times., i.e., 2.5.times.10.sup.-9 M+10.sup.-8 M LADEA+10.sup.-7 M **climbazole** , which resulted in this combination inhibiting TG1 levels to 72% of control. **Retinol**, fatty acid amides and **climbazole** therefore act synergistically to repress keratinocyte differentiation in an analogous manner to the effect of retinoic acid.

DETD

	% w/w
Retinol	0.15
Palmitoyl-monoethanolamide	0.1
Climbazole	2
Ethanol	40
Antioxidant	0.1
Perfume	qs
Water	to 100

DETD

	% w/w
Retinol	0.01
Linoleoyl monoethanolamide	0.1
Climbazole	0.1
Silicone oil 200 cts	7.5
Glycerylmonostearate	3
Cetosteryl alcohol	1.6
Polyoxyethylene-(20)-cetyl alcohol	1.4
Xanthan gum	0.5
Parsol 1789	1.5
Octyl methoxycinnate (PARSOL MCX)	7
Perfume	qs
Color	qs
Water. . .	